Human Health and Ecological Risk Assessment Training

February 22-26
Brasilia, Brazil

Summary: Environmental risk Assessment plays a unique role in serving the needs of various international programs through incorporating, integrating, and coordinating the use of scientific information as a foundation for regulatory decision-making. Risk assessment is an ever-evolving process that significantly impacts human health, food safety, economics, ecological systems, and social decision-making. The United States Environmental Protection Agency (EPA) is a global leader in conducting state-of-the-science risk assessments, and its publications are often the first to apply new risk assessment guidelines, scientific methods, and data. This course will offer training in the primary areas of risk assessment (i.e., hazard identification, dose-response assessment, exposure assessment, and risk characterization). It also will briefly cover risk communication and management concepts because outreach to the public and other stakeholders is essential for the successful implementation of a risk assessment, and ultimately, an environmental decision. This training course will represent the culmination of knowledge-sharing among science experts in the field of human health and ecological risk assessment and exposure assessment. The modules characterizing exposure assessment will be repeated in Session 1 and 2. Case studies demonstrating applications of risk assessment in different settings will also be discussed.

Day 1: Morning Session (8:00 am to 12:00 pm
Joint Human Health and Ecological Risk Assessment Sessions

8:00 am **Introductions and Brazilian Perspective**

- Luis Eduardo Pacifici Rangel, Ministry of Agriculture/MAPA, Secretary of Plant and Livestock Defense
- Caio Augusto de Almeida, Health Surveillance Agency/ANVISA, General Manager of Toxicology
- Karina Cham, Brazilian Environmental Institute/IBAMA, Environmental Analyst
- Guilherme Guimarães, Brazilian Crop Protection Association/ANDEF, Regulatory Manager

8:20 am **Introduction to Risk Assessment at EPA** The objective of this course is to provide participants with a basic introduction to the fundamental concepts and terminology associated with risk assessments (e.g., human health, ecological, microbiological). How the risk assessment process is related to and informs risk management policies also will be covered. Examples of how the Federal Government applies the risk assessment paradigm will be provided, including real-world examples of human health and ecological risk assessments. **Drs. Allan Davis and Jeff Herrick**

9:20 am **Risk Assessment Topics of Interest for Brazil**
Discussion of current risk assessment issues faced by organizations located in Brazil. Speakers may include representatives from ANVISA, ANDEF, and IBAMA.

10:00 am Break

10:15 am **Laws and Regulatory Foundations for Risk Assessment**
The objective of this course is to provide participants with knowledge of the specific legal and regulatory underpinnings of risk assessment under United States Environmental Protection Agency programs. Specific laws covered include: the Clean Water Act (CWA); the Federal Insecticide, Fungicide and Rodenticide Act, the Federal Food Drug and Cosmetic Act/Food Quality Protection Act (FFDCA/FQPA) and Executive Order 13045. Some State-specific regulatory information also will be briefly covered. **Mr. Ben Harrison, JD**

11:15 pm **Data requirements for pesticides**
Under FIFRA, a suite of data is required of pesticide registrants. These data define the pesticide's physical, chemical and fate properties, measured residues in crops and environmental matrices as well as the toxicity of the pesticide to humans, non-target organisms (e.g., birds, fish) and plants. This talk will provide a brief overview of the data requirements. **Jeff Dawson, Mike Doherty, Kristina Garber**

Lunch 12:00 pm – 1:00 pm

Day 1: Afternoon Session (1:00 pm – 5:00 pm)
Human Health Risk Assessment Session

1:00 pm **Overview of Human Health Risk Assessment - Dr. Ila Cote**
The objectives of this course are to provide participants with knowledge of the fundamentals of risk assessment, especially as they pertain to human health. Specific aspects of risk assessment covered will include the four elements of a risk assessment (hazard identification, dose-response assessment, exposure assessment, and risk characterization) and common terminology used in risk assessments. Hazard identification will cover the use of epidemiologic and toxicologic studies as well as toxicokinetic, toxicodynamic, and mechanistic studies to identify the proposed causative agent, including use of the EPA Cancer Guidelines and Noncancer Framework for evaluating causality. Dose-response assessment will cover an introduction to the development of Reference and Risk Values. Additionally, the application of Benchmark Dose (BMD) Modeling and the BMD Technical Guidance document and Mode of Action will be discussed. This will be followed by a comparison of the types of risk assessments and their uses (e.g., safety assessments, biologically-based dose responses). Typical risk assessment extrapolations used to estimate human health relevance from lab data will be presented. Exposure assessment will cover the various aspects of exposure to an agent or stressor. In general, exposure is characterized by identifying the agent, route, dose, and frequency. Finally, risk characterization will describe the integration of the previous elements to derive an estimate of risk. Discussions will include the various uncertainties and assumptions involved in the risk assessment process.

2:30 pm Break

3:00 pm **Quantitative Methods and Models – Dosimetry and PBPK Concepts - Dr. Ila Cote**
The objectives of this course are to provide participants with knowledge of dose, route, and species extrapolation methods, including default dosimetry methods (e.g., dosimetry adjustment factors (DAFs), chemical specific adjustment factors (CSAFs), body weight scaling, etc.), and the associated uncertainties. Approaches to derive reference values will also be presented. In addition, participants will gain insight into the fundamental concepts of physiologically based pharmacokinetic (PBPK) modeling (e.g., pharmacokinetics, underlying physiology, model structure, and methods of model parameter estimation). Methods to evaluate PBPK models for use in risk assessment (e.g., extrapolation and internal dose estimates) will also be presented.

5:00 pm **Adjourn**

Day 2: Morning Session (9:00 am – 12:00 pm)

Human Health Risk Assessment Session

9:00 **Understanding and Characterizing Uncertainty and Variability - Dr. Ila Cote**
The objectives of this course are to provide participants with knowledge to differentiate between uncertainty and variability, understand how both of these are addressed in human health risk assessment as conducted by EPA (and in particular how NCEA addresses these in IRIS assessments), and understand how they ultimately inform derivation of the toxicity reference values used in risk assessments. Application of the different uncertainty factors (UFs) implemented by NCEA in the derivation of toxicity values, and the general criteria employed to determine a UF, are an integral part of this course. Examples and case studies of the use of the various UFs are presented.

10:00 **Understanding the Risk assessment Basis for Pesticides - Drs. Jeff Dawson and Michael Doherty**

Pesticides and herbicides are critical in protecting public health and various agricultural crops. Approval of pesticides for agricultural or public health is complex process. Risk assessment plays critical role in pesticide approval processes and in setting the tolerance level of pesticide in various food commodities. In this part of the course, the student will receive hands on training on the application of risk assessment to assess and ensure the safety of pesticides. The procedure of setting of pesticide tolerance will be studied. The student will be able to compare the pesticide tolerance values across various international organizations.

10:30 **Break**

11:00 **Understanding the Risk Assessment Basis for Pesticides - continued**

12:00 pm – 1:00 pm Lunch

Day 2: Afternoon Session (1:00 pm – 5:00 pm)
Human Health Risk Assessment Session

1:00 pm **Case Study in Pesticide and Risk Assessment - Drs. Jeff Dawson and Michael Doherty**

A case study will be presented based on the recently completed risk assessments for the herbicide, 2-4-D. Information related to this analysis can be found at [HYPERLINK "http://www.regulations.gov"] under Docket ID EPA-HQ-OPP-2012-0330-0004 and also EPA-HQ-OPP-2014-0195. On overview of each aspect of the process will be presented with background information on each element including hazard assessment, dose response evaluation, dietary exposure and risk, exposure and risks for the general population not through diet, and exposures and associated risks for workers who use pesticides.

5:00 pm **Adjourn**

Day 3: Morning Session (9:00 am – 12:00 pm)
Exposure Assessment – Joint Session

9:00 am **General Concepts and Approaches for Quantifying Exposure – Jeff Dawson, Mike Doherty, Kristina Garber** Participants will be introduced to the various components of an exposure assessment as well as key terminology. Fundamentals that will be covered include: intake,

uptake, and dose; applied, potential, internal, and biologically effective dose; acute, average daily dose, and average lifetime dose; and dermal, oral, and respiratory dose. This course will transition into selecting the approach for quantifying exposure/dose, as well as determining the appropriate type and scope of the study are important first steps in planning an exposure assessment. This course is designed to explore the various approaches that may be used to measure or model exposure, including point-of-contact measurements, scenario evaluation methods, and dose reconstruction approaches. The purpose and utility of these approaches as well as their strengths and weaknesses will be covered. Participants will also be introduced to the types (e.g., deterministic or probabilistic) and scope (e.g., single or multiple chemicals; national-scale, or specific location or industry). The use of exposure descriptors in the exposure assessment planning process will also be discussed.

9:45 am Break

10:15 am **Fate and Transport - Kristina Garber**
The objective of this module is to give participants an overview of the factors that are important when assessing the fate of contaminants, starting from their point of release until they reach "receptors" (i.e., adults, children, sensitive subpopulations, and other exposure receptors) at the "site of exposure" (a residence mostly). Figures will show potential pathways of movement from source to receptor, and how the ultimate appearance of contaminants in "exposure media" (air, soil, water, food) lead to exposure. The important concept of transfer of contaminants between media - air to soil, soil to plant, water to fish, etc. - will be described. Concepts of partitioning and first order degradation will be presented, and common parameters such as Henry's Constant, octanol water (or octanol air, or organic carbon, and other) partition coefficients will be defined. The module will conclude with simple paper and calculator exercises on partitioning and first-order decay.

12:00 pm – 1:00 pm Lunch

Day 3: Afternoon Session (1:00 pm - 5:00 pm)
Exposure Characterization Specific to Health
Human Health Assessment Session

1:00 pm **Developing Exposure Scenarios - Drs. Jeff Dawson and Mike Doherty**
The objectives of this course are to provide participants with a basic foundation in the concepts and principles of human exposure assessment Participants will be introduced to the various components of an exposure assessment as well as key terminology. Fundamentals that will be covered include: intake, uptake, and dose; applied, potential, internal, and biologically effective dose; acute, average daily dose, and average lifetime dose; and dermal, oral, and respiratory dose. This course will familiarize participants with EPA's existing and soon-to-be updated *Exposure Assessment Guidelines* and other key exposure assessment resources. Pesticide specific examples will be used to illustrate the concepts. Detailed information will be presented regarding how the use of scenario-based exposure assessment is a core element of the U.S. regulatory process. The information provided will address the following:

- Dietary risks for different subpopulations
- Residential use patterns
- Occupational tasks across agriculture and other pesticide markets
- Ecological risks for different taxa

2:30 Break

3:00 pm **Developing Exposure Scenarios - continued**

5:00 pm **Adjourn**

Day 4: Morning Session (9:00 am – 12:00 pm)
Exposure Assessment – Joint Session - Jeff Dawson, Mike Doherty, Kristina Garber,

9:00 am **Exposure modeling in water**
EPA's OPP uses simulation models to estimate pesticide concentrations in water that may be consumed by humans as drinking water or may result in exposures to non-target aquatic organisms. This session will provide an overview of the aquatic exposure models[1].

9:45 pm Break

10:15 am **Estimating exposures via spray drift transport**
This session will discuss methods for estimating spray drift transport of pesticides. The AgDRIFT[2] model will be discussed.

11:15 am **Monitoring data**
For many pesticides, monitoring data are available for various media, including water and food. This session will discuss types of monitoring data and how they may be incorporated into the characterization of pesticide exposure to humans and the environment.

Lunch **12:00 pm – 1:00 pm**

Day 4: Afternoon Session (1:00 pm - 5:00 pm)
Human Health Session

1:00 pm **Obtaining and Using Exposure Factor Data - Jeff Dawson and Mike Doherty**
The objective of this course is to provide participants with a basic introduction to the fundamental concepts and terminology associated with risk assessments (e.g., human health, ecological, microbiological). How the risk assessment process is related to and informs risk management policies also will be covered. The mission and organizational structure of EPA's Office of Research and Development (ORD) also will be covered, focusing on how ORD performs research to identify and understand current and future environmental problems and how this research informs EPA's risk assessment goals. Finally, examples of how the Federal Government applies the risk assessment paradigm will be provided, including real-world examples of human health and ecological risk assessments.

2:45 pm Break

3:15 pm **Interpreting Biomonitoring Data and the Use of Simple Pharmacokinetic Models to Characterize Dose - Dr. Jeffery Davis**
The widespread acceptance and use of the CDC's NHANES (National Health and Nutritional Examination Surveys) database, which includes measurement of contaminants in blood and urine, has led to a greatly expanded understanding of general population exposures in the United States.

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[1] For a description, go to: http://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/models-pesticide-risk-assessment#aquatic

[2] For a description, go to: http://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/models-pesticide-risk-assessment#agdrift

Biomonitoring data is the most direct measure of exposure, and can be used to characterize exposure in a contaminated or general background situation. This module will discuss biomonitoring data in general, but with a focus on what is offered by NHANES data. Related topics will also be discussed. One such topic is the use of simple pharmacokinetic models to infer intakes from biomonitoring data. In other words, a urine or blood measurement can be traced back to an intake with the use of simple pharmacokinetic models that can be applied to a host of contaminants with a minimal amount of data. Another topic is the use of these measurements in a framework termed, "biomonitoring equivalents". Here, blood or urine concentrations can be related to the potential for a health impact. The best example here is blood lead, but recently, this concept has been expanded to a host of additional contaminants.

5:00 pm **Adjourn**

Day 5: Morning Session (9:00 am – 12:00 pm)
Human Health Risk Assessment Session

9:00 am **Case studies focused on human health risk of pesticides - Drs. Jeff Dawson and Mike Doherty**

This section will provide additional case studies with a focus on emerging scientific and regulatory issues. Three to four examples will be identified and the each will be addressed from a lifecycle perspective including how the issue was identified, the resolution of the issue and its scientific basis, the regulatory implications, and other related activities such as peer review processes.

10:30 am **Break**

11:00 am **Case study focused on human health risk of pesticides (Continued)**

Lunch 12:00 pm – 1:00 pm

Day 5: Afternoon Session (1:00 pm – 2:30 pm)
Joint Session – Discussion, Questions and Answers

1:00 pm **With Focus On Future Collaboration and Scientific/Regulatory Harmonization**

2:00 pm **Wrap up, concluding remarks.**

2:30 pm **Adjourn**